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THE RESULTS OF PITUITARY TUMOR OPERATIONS *

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During the past 15 years, 106 pituitary tumors (66 adenomas and 40 craniopharyngiomas) have been surgically treated in the First Surgical Division of the Kyoto University Hospital.

The results of the operations are reported in this paper.

A. ADENOMAS

57 out of 66 were chromophobe adenomas and the remaining 9 were adenomas with acromegalic syndrome. Although the latter are generally believed to be eosinophilic, they were in no case of our series typical eosinophilic, but all mixed adenomas.

The tumors were always operated on by a transfrontal and intradural approach. There was no case in which a transsphenoidal route was adopted. The operations were done 71 times in all.

Items of the operations are given in Table 1.

a) Early results of operations

As is shown in Table 2, case mortality is 10.6% in all adenomas and 12.3%

Table 1 Modes of the operations performed for pituitary adenomas

		Chromophobe adenomas	Acromegaly	Total
Transfrontal intradural approach	Collapsing of tumor by intracapsular enucleation or by evacuation of cystic content	55	7	62
	Partial removal	3	0	3
	Exploratory operation	1	2	3
Fronto-temporal approach (collapsing of tumor)		2	0	2
Torkildsen's operation		1	0	1
Total		62	9	71

Table 2 Immediate results of operations

	Improved	Uneffected	Aggravated	Died	Total
Chromophobe adenomas	41	11	3	7	62
Acromegaly	4	5	0	0	9
Total	45	16	3	7	71

* Dedicated to Prof. Dr. Hiromu Ito in commemoration of his 70th birthday (July 29, 1955)

in chromophobe adenomas. The results are nearly the same as those reported by Grant, Bakey (Olivecrona), Davidoff and Horrax, but much worse than those of Hirsch, who is doing exclusively transsphenoidal operations, and those of Cushing

Table 3 Opera ive mortality of pituitary adenomas

Author	Tumor	Case mortality (%)
Cushing (Henderson)	Adenomas in all	5.0±1.2
Grant		11.9±3.9
Hirsch		5.4±1.4
Araki		10.6±3.8
Olivecrona (Bakey)	Chromophobe adenomas	11.3±1.9
Davidoff		15.4±3.7
Horrax		14.1±3.2
Araki		12.3±4.4

(Table 3). The death was in all cases due to diencephalic disturbances, showing hyperthermia and loss of consciousness, and took place in most cases within 15 hours after operation.

In discussing the mortality of pituitary tumor operations,the occurrence of extrasellar extensions should be taken into consideration. According to Jefferson, a pituitary tumor is said to have an extrasellar extension, if the extrasellar portion of the tumor is as large as or larger than the intrasellar portion. *

The incidence of such tumors is reported to be 14% of all adenomas (Jefferson). It is 15.2% in our series. It has been experienced by many neurosurgeons that the results of operations in those pituitary tumors with extrasellar extensions are extremely unfavorable, the immediate mortality being around 35%.

In our series, there are 10 cases of adenomas with extensions, of which 5 died after operation (50% mortality). However, if such adenomas are excluded, the operative mortality is 4.3% in our series, 2% in Jefferson's, 6.4% in Bakey's (Olivecrona) and 3.9% in Horrax's series respectively, nearly the same rate as that in Cushing's or of Hirsch's series.

Henderson and Bakey reported that the mortality is higher in the patients of the advanced stages as evidenced by the total blindness of unilateral or bilateral eyes. All of our fatal cases were operated on in such delayed periods. It is our impression that more patients come too late to operation in this country than in others. Another fact, which seems noticeable in this country, is that more adenomas are cystic.

* The diagnosis of an extrasellar extension by this criterion can certainly be made at autopsy, but not always at operation, since the operative exposure is usually not wide enough to obtain the full view of a tumor. Even in such cases, if there were uncommon symptoms suggesting an extension, we made the diagnosis, e. g. of a hypothalamic extension in the presence of a marked hydrocephalus, polyuria, polydipsia, somnolence and convulsions and the diagnosis of a protrusion into the cavernous sinus in the presence of distinct paralysis of the oculomotor and / or trigeminal nerves. Thus the occurrence of an extrasellar extension in surviving patients is frequently presumptive.

According to Henderson and Vaughan, cystic adenomas are encountered in about 15% ,whereas they are 63.2% in our series, even when the adenomas with gelatinous content are excluded. It has been believed that cystic adenomas are better effected by operation, but tend to recur earlier and are refractory to X-ray treatment. In our series, recurrence within 2 years after operation seemed to have taken place somewhat more frequently in cystic adenomas.

Recurrence was experienced in 26 cases (39.4%), including the cases of later death, the rate being nearly the same as 46% of Cushing. Postoperative improvement of the vision was excellent in those patients who were operated on within 6 months after the onset of the visual symptoms (Table 4).

Table 4 Postoperative recovery of vision in relation to years elapsing after the onset of visual symptoms

Years after the onset of symptoms	Number of cases	Postoperative visual acuity (unilateral or bilateral eyes)	
		Over 1.0	Over 0.6
Within ½	7	6	6
½— 1	11	4	8
1— 2	17	6	11
2— 3	8	2	3
3— 4	3	1	1
4— 5	4	1	2
5—10	8	2	5
Total	58	22	36

Generally speaking, (i) it is possible for the vision of more than 0.1 before operation to recover to more than 0.6, sometimes 1.0 after operation, (ii) the vision of less than 0.1 before operation can not be expected to recover to more than 0.6 and (iii) totally blind eye never recovers by operation.

Postoperative enlargement of the visual field is mostly parallel with the recovery of the visual acuity, but tends to occur somewhat earlier than the latter. Headaches, nausea and vomiting disappeared after operation in nearly all cases, irrespective of the occurrence of visual improvement.

Endocrine disorders are not favorably effected by operation.

b) Results of recurrence operations.

There are 12 cases in which operations were done for recurrent tumors. The results are not encouraging; improvement in only 4, symptoms unaltered in 6 and postoperative death in 2.

Henderson states in reviewing Cushing's series that visual improvement can be expected only in those cases where reoperation has been done within 3 months after the onset of recurrent symptoms.

Just within this period came to reoperation all the 4 cases in our series, in which the vision recovered again. Remaining 8 patients were reoperated on too late, thus the results being unsatisfactory.

c) Effect of postoperative X-ray therapy.

To 20 cases a postoperative X-ray irradiation in a large dose was given. In no case any remarkable improvement was noticed in both the visual acuity and the visual field. Also it is not definitely evidenced that the later course of the illness has been favorably influenced on by the irradiation, although the early recurrence might have been somewhat inhibited.

d) Follow-up results (Table 5).

Table 5 Follow-up results of pituitary adenoma operations

Years after operation	Chromophobe adenoma		Acromegaly	
	Working	Unable to work	Working	Unable to work
0— 1	2	2	1	0
1— 2	1	1	0	0
2— 3	3	1	0	1
3— 4	4	0	0	1
4— 5	1	0	0	0
5— 6	1	1	0	0
6— 7	0	0	0	0
7— 8	1	1	0	0
8—10	0	0	0	0
10—11	0	1	1	0
11—12	0	0	0	0
12—13	2	1	0	0
13—18	0	0	0	0
18—19	1	0	0	0
Total	16	8	2	2

Of 59 cases which survived operation, 42 gave answers to the inquiry. 28 patients are alive and 14 dead. Of the living 28, 18 are working and the remaining 10 are unable to work due to impairment of vision, reappearance of headaches and convulsions etc. There are 16 patients with a more than 3 year survival. Of these 11 are working and 5 unable to work.

The death in 14 cases occurred at various periods after operation; 3 within 1 year, 5 between 1-2 years, 2 between 3-5 years and 4 between 5-8 years. The cause of death is a presumable recurrence of tumor in 10 and some other illness in 4.

B. CRANIOPHARYNGIOMAS

Craniopharyngiomas in non-autopsy cases have been identified by histologic findings of the tissue specimen taken at operation or by supra- or intrasellar calcification on X-ray films, or by the presence of cholesterine chrystals in the cystic content. Of 40 cases of craniopharyngioma in our series, 20 are cystic and 10 solid.

Routinely we have approached the tumor by a transfrontal and intradural route, evacuated the cyst and removed the solid mass of the tumor by curettage as much as possible. However not infrequently the tumor is found to be concealed behind

the optic chiasm, so that it can not be reached by this approach.

In such cases, a cortical incision is immediately made at the vertex of the frontal lobe into the lateral ventricle, exposing the tumor bulging through the foramen of Monro. Then the tumor is incised and evacuated. The usually accompanying hydrocephalus makes the procedure quite easy. The incision of the floor of the third ventricle results usually in no hyperthermia, because it is atrophied as thinly as a paper by the compression of the tumor.

The frontal cortical incision should be made as near as possible to the midline in order to avoid the possible sequela of hemiplegia.

The operation by a transventricular approach should not go further than the evacuation of a cyst. Any attempt to remove the solid mass of the tumor is dangerous. In cases of solid craniopharyngiomas with obstructive hydrocephalus, Torkildsen's ventriculo-cisternostomy is preferred.

Drainage of the cyst into the third ventricle by means of a small tube made of rubber or vinyl has been recommended by some authors but never used in our Clinic.

For 40 craniopharyngiomas, we have done operations 43 times, the items being shown in Table 6.

Table 6 Modes of the operations performed for craniopharyngiomas

		Improved	Uneffected	Died	Total	
Transfrontal intradural approach	Exploratory operation	0	2	3	5	
	Evacuation of cyst	10	5	2	17	29
	Partial removal	3	1	3	7	
Transventricular approach	Exploratory operation	0	3	0	3	
	Evacuation of cyst	4	1	1	6	10
	Partial removal	0	0	1	1	
Tapping of cyst without craniotomy		0	1	0	1	
Torkildsen's operation		0	3	0	3	
Total		17	16	10	43	

a) Early results of operations.

The visual acuity and the visual field were improved in 17 cases and unaltered in 16. Death within a week after operation occurred in 10, and the immediate mortality is 25%. The cause of death seemed to be the diencephalic disturbance. Curiously enough, however, hyperthermia was observed less frequently than after operations for adenomas. There were 4 additional deaths, occurring around a month after operation. Thus the total mortality during admission in the Clinic is as high as 35%, nearly the same as that reported by Love. It may be a matter of course

that operation is more favorable for a cystic craniopharyngioma than for a solid, the improvement of the visual disturbance being better and the mortality lower in the former.

Any operation for a craniopharyngioma, which is solid and extensively calcified, usually aggravates rather than ameliorate the symptoms.

The patients with signs of severe involvement of neighboring nervous structures tolerate operations poorly, although the operative mortality is not always high in the patients of craniopharyngioma with severe visual impairment contrary to the similar patients of adenoma.

b) Reoperations.

Reoperation was done in 3 cases, because of recurrence of symptoms, with recovery in 1, no change in 1 and death in 1.

c) Postoperative irradiation.

To 5 cases a postoperative irradiation in a large dose was given without any remarkable benefit.

d) Follow-up results (Table 7).

Table 7 Follow-up results of craniopharyngioma operations

Years after operation	A Working	B Unable to work	C Ill in bed
0— 1	2	2	1
1— 2	1	0	0
2— 4	0	0	0
4— 5	1	1	0
5— 8	0	0	0
8— 9	1	1	0
9—10	1	0	0
10—11	0	0	0
11—12	1	1	0
Total	7	5	1

From 23 of the 25 cases which survived operation, informations were available as to the outcome of the patients. 13 are alive and 10 dead. Survival periods after operations in these 10 fatal cases were 4, 5, 9, months, 1 year (2 cases), 1y2m, 1y8m, 3y1m,4y10m, 9y2m repectively; thus 3 of these fatal patients survived operation for more than 3 years. The cause of death seemed to be the progressive growth of the tumor in all cases.

Periods after operation in the 13 patients alive at present are given in Table 7. 7 patients in group A of the Table are working and 4 of them are living for more than 3 years after operation. 5 patients in group B are unable to work due to visual disturbances. 1 patient in group C is ill in bed because of headaches, convulsions besides visual disturbances.

It is somewhat encouraging for us that 7 out of 40 patients of craniopharyngioma were (or are) alive for over three years after such an incomplete operation as a mere evacuation of a cyst and that 3 patients are working well for over 8 years

after operation.

SUMMARY

1) Of 106 pituitary tumors operated on in our Clinic, there are 66 adenomas (57 chromophobe and 9 mixed) and 40 craniopharyngiomas.

2) Early results of adenoma operations. The tumor was reached routinely by a transfrontal and intradural approach. Case mortality is 10.6% in all adenomas and 12.3% in chromophobe adenomas. Herein included are the adenomas with extrasellar extensions, which make up 15% (10 cases) of all adenomas and show a high mortality of 50%. If they are excluded from the series, the mortality is 4.3%.

3) It is to be noted regarding adenomas that (i) more patients came to operation in the advanced stages as evidenced by the total blindness of unilateral or bilateral eyes and (ii) more adenomas (63%) were cystic than in foreign countries.

4) Postoperative recovery of the vision was excellent in those patients who were operated on within 6 months after the onset of visual symptoms. Headache, nausea and vomiting disappeared after operation in all cases. To 20 cases a postoperative X-ray irradiation in a large dose was given without any remarkable benefit.

5) Follow-up results of adenoma operations. Informations were obtained from 42 patients; 11 are working and 5 alive but unable to work for more than 3 years. 14 patients died at various periods after operation.

6) For 40 craniopharyngiomas, operations were done 29 times by a transfrontal and intradural route and 10 times by a transventricular route. Also Torkildsen's operation was done in 3 patients.

7) In the early period after operations for craniopharyngioms, 17 patients improved the vision and 10 died within a week and additional 4 died around a month, thus the mortality during stay in the Clinic being 35%.

8) However it is somewhat encouraging that out of 10 patients who lived for over 3 years after operation, 4 are working well.

Thanks should be expressed to Dr. Naoki Kageyama for his aid in obtaining follow-up informations.

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和文抄録

脳下垂体腫瘍の手術成績

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本年2月迄に私のところで手術した脳下垂体腫瘍が106例ある．その中66例が腺腫で，40例が Craniopharyngioma である．これらの患者の術後早期の成績及び遠隔成績を調査した結果を報告する．

A 腺腫

66例中57例が chromophobe 腺腫であり，9例が acromegaly を伴つた腺腫である．(第1表)．これらに対して，我々は専ら transfrontal, intradural の経路による手術を71回行つているが，手術の内訳は第1表の如くである．

a) 術後早期の成績． (第2表)

死亡率は腺腫全体として10.6%，chromophobe 腺腫だけでいうと12.3%であつて，これを外国の諸家の成績と比較すると，(第3表)，Cushing や Hirsch より悪いが，他の人の成績とは似たようなものである．尚手術死亡率で問題になるのは extrasellar extension をもつた腺腫で，これはあまりハツキリしない概念ではあるが，外国の報告でも，我々の例でも大体腺腫の15%位に認められて居り，その手術死亡率は大変高く，35%位といわれるが，我々の例でも50%の死亡率である．この extrasellar extension の例を除くと，誰の成績でも略一様に5.0%前後となり，Cushing と似たような数字になる．尚外国の場合と多少異るところは，一眼盲乃至両眼盲の患者，即ち症状の進んだ患者の多いこと(これは手術成績を悪くするものであるが)，それと嚢腫性の腺腫の多いこと63% (他国15%)，(これは手術直後の恢復が早い代りに，再発も早く，又レ線治療も効かないものである)，この2点である．

我々の経験からいつて，症状初発後半年以内というような早期の症例では，手術後の視力の恢復がよい．(第4表)，又術前の視力0.1以上であれば，術後0.6以上に迄恢復し得る．術前盲の眼は手術により殆んど恢復しない．(第5表)．又術前にあつた頭痛，悪心，嘔吐等は殆んど全例に消失しているが，内分泌障害は大多数では恢復しない．

b) 術後レ線照射.

20例に大量照射を行つたが，効果があつたとは思わない．

c) 追求成績 (第5表)

手術死亡例を除いた59例中，消息の判明した42例について見るに，現在迄生存28例，死亡14例である．生存28例中18例は仕事に就事して居り，残りの10例は働けない儘である．死亡14例の死因は10例が再発，他の4例は別の原因である．

B Craniopharyngioma

(第6表)．手術法は原則として腺腫の場合と同様であるが，腫瘍が視束交叉よりも後方にあつて，前からは到達出来ない時には，側脳室を開いて，モンロー氏孔から腫瘍に到達する．又このような場合には，必ず脳内水腫が続発しているから，それを軽減する目的で，Torkildsen 手術を行つた例もある．これらの手術を我々は40例に対して43回行つている．術後早期の成績は軽快(これは主として視力，視野の改善である)，これが17，不変16，死亡10である．従て死亡率25%である．それに手術後1月前後になつて死亡した4例があるので，入院中死亡35%ということになり，相当高い死亡率であるが，これも外国の報告と大体同様な数字である．術後レ線照射を行つたのが5例あるが，効果があつたとは思われない．

追求成績 (第7表)

入院中死亡15例を除き，残りの25例の中，消息の判明せるものが23，この中其後の死亡10である．この死亡10例の中には，手術後3年以上生存したものが3例ある．生存13例の生存期間は表の如くで，職場で働いている7例中の3例は術後3年以上を経過している．これから見ると，単なる嚢腫切開だけで3年以上の生存が可能であり，時には8—12年の間仕事に従事出来る場合もあるので，この腫瘍の手術は絶望的なものではない．